

EDITORIAL COMMENT†

SEMLIKI FOREST VIRUS

During the course of a field investigation on the epidemiology of yellow fever, a hitherto unknown neurotropic virus was isolated from mosquitoes by Smithburn¹ and associates of the Yellow Fever Research Institute, Entebbe, Uganda.

About 130 female *Aedes abnormalis* mosquitoes caught in the Semliki Crown Forest were emulsified in 4 c.c. 10 per cent normal human serum and the emulsion filtered through a Seitz EK asbestos pad. Samples (0.03 c.c.) of the resulting filtrate were inoculated intracerebrally into 6 normal adult white mice. All mice remained well till the 27th day when one became paralyzed in the hind legs. This mouse was sacrificed and its brain used for intracerebral inoculation of a second group of 6 mice. All mice of the second group became ill on the 4th day. Four were then sacrificed for subinoculation tests. The other 2 died on the 7th day.

There were still greater increases in virulence on subsequent brain-to-brain passage. By the 160th passage the virus had become so virulent that it caused symptoms within 24 hours after intracerebral inoculation, death usually occurring within 48 hours. It was found that 5 to 20 intracerebral MLD of the passage virus were required to cause death by subcutaneous or intraabdominal inoculation, and from 1,000 to 10,000 MLD to cause death by intranasal instillation. By the 99th mouse passage the virus had acquired a demonstrable intracerebral pathogenicity for guinea pigs and rabbits, but was not sufficiently pathogenic to produce illness upon extraneural inoculation. By the 132nd mouse passage the virus had acquired a demonstrable intracerebral pathogenicity for rhesus monkeys, but was still non-pathogenic for monkeys if given by the subcutaneous route. Given extraneurally the virus stimulates the production of circulating antibodies in guinea pigs, rabbits and monkeys, as shown by serum protection tests on mice. Intracerebral pathogenicity and extraneural antigenicity were also demonstrated with 5 species of wild primates captured in neighboring regions of the Semliki Crown Forest.

The virus can be readily cultivated in the developing chick embryo, and suffers very little loss of potency if dehydrated in the Flosdorff-Mudd apparatus. Ultrafiltration experiments indicate that it is probably the smallest virus thus far discovered. Cross-neutralization tests with specific immune serums have shown that the virus is not identical with any known filterable virus thus far described, with the possible exception of that of

Russian spring-summer encephalitis, not yet tested.

In mice injected intracerebrally the virus appears in the circulating blood in remarkably high concentration long before the onset of symptoms. In one titration of 5 pooled serums from mice still apparently well, 16,500,000 infective units per c.c. were demonstrated by intracerebral tests. After symptoms develop, the brain titer is usually at least 100 times that of the serum titer. The virus is also present in considerable quantities in the heart muscle, lungs, liver, spleen and all other tissues thus far tested. The titer is relatively high in the kidneys, suggesting that the virus is both neurotropic and nephrotropic.

The only constant macroscopic lesion seen at autopsy in mice, guinea pigs, rabbits or monkeys is hyperemia of the brain. In every brain thus far studied minute foci of necrosis and local infiltrations were found, lesions not unlike those described by Watson² in equine encephalomyelitis. Minor renal lesions were also present in most animals. All other visceral tissues escaped demonstrable injury.

Serums from 20 species of African wild animals have thus far been tested for the presence of specific antibodies. Humoral immunity was present in 24 of the 65 primates (6 different species) tested, but was not demonstrable in non-primates. Serums from 313 human beings were similarly tested, 47 of whom gave positive reactions. The percentage of positive reactions varied from 7.9 per cent to 32 per cent in different regions, and was usually much higher in adults than in children.

It is not yet apparent that the natural virus causes recognizable illness in man or primates, nor that there are any objective sequelae other than specific antibody production. Mosquito transmission is suspected, though not yet fully established.

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REFERENCES

1. Smithburn, K. C., Mahaffy, A. F., and Haddow, A. J., *J. Immunol.*, 49:141, 159 (Sept.), 1944.
2. Watson, D. W., and Smadel, J. E., *Proc. Soc. Exp. Biol. and Med.*, 52:101, 1943.

Caïus Julius Caesar (B. C. 100-44).—Historical verification that Caesar was an epileptic seems to rest upon the authority of Plutarch and Suetonius. Both speak of repeated attacks, one having occurred just before the battle of Thapsus. Whenever he felt an epileptic seizure coming on, Caesar would try to cover his face. In the opinion of one writer the contemporary bust of Caesar quite plainly indicates the *Facies Epilepticus*, while another says that the iconography of Caesar proves the absence of facial anomalies.—Warner's *Calendar of Medical History*.

A man stricken with tuberculosis is just as much of a loss to the nation for whom he might otherwise be working or fighting as a man blasted with shrapnel.—Lt. Comdr. Emil Bogen, M.C., U.S.N.R., *Amer. Rev. Tbc.*

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